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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,170	04/16/2004	Ciaran N. Cronin	SYR-HDAC-5004-C1	8535

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
05/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,170	CRONIN ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,8,10,25,26,28,31,44-46 and 49-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8,10,25,26,28,31,44-46 and 49-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 March 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/7/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 7-8, 10, 25-26, 28, 31, 44-46, and 49-52 are pending in the application.

[2] Applicant's amendment to the claims, filed on 3/5/07, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Applicant's amendment to the specification, filed on 3/5/07, is acknowledged.

[4] Applicant's amendment to the drawing figures, filed on 3/5/07, is acknowledged.

[5] Applicant's arguments filed on 3/5/07 in response to the Office action mailed on 9/5/06 are acknowledged. Applicant's arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[6] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Information Disclosure Statement

[7] All references cited in the information disclosure statement (IDS) filed on 2/7/07 have bee considered by the examiner. A copy of Form PTO/SB/08 is attached to the instant Office action.

Specification

[8] The specification is objected to as being inconsistent as identifying the amino acid sequence of the atomic coordinate listing of Figure 3 as SEQ ID NO:5. According to Figure 3, the first amino acid in the listing is Gly. However, the paper copy of the sequence listing identifies Met as the first amino acid of SEQ ID NO:5. Also, the specification notes that structure coordinates are not reported for some residues (specification pp. 28-29, paragraph 120). As such, it is unclear how the amino acid sequence as set forth in Figure 3 can be that of SEQ ID NO:5. Appropriate correction is required.

[9] The amendment filed 3/5/07 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: changing the range of amino acids for which structure coordinates are not reported from 1-12 to 1-11 for chain A. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112, Second Paragraph

[10] Claims 8, 26, and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8, 26, and 46 are unclear in the recitation of "the protein crystallizes as a trimer." According to applicant, the disclosure in the specification (p. 28, paragraph 118) that "[d]uring structure determination...it was realized that the asymmetric unit

comprised three HDAC-2-Zn2+-TSA molecules" is intended to mean that SEQ ID NO:5 crystallized as a trimer. According to Stedman's Online Medical Dictionary, the term "trimer" is defined as "[a] compound...made up of three components." Thus, the recitation of "the protein is present...as a trimer" suggests that the protein is made up of three components. However, a skilled artisan would recognize that the specification's disclosure of "[d]uring structure determination...it was realized that the asymmetric unit comprised three HDAC-2-Zn2+-TSA molecules" means the crystal has three molecules of HDAC-2-Zn2+-TSA per asymmetric unit – not that the protein of the crystal was made up of three components. It is suggested that applicant clarify the meaning of the noted phrase.

Claim Rejections - 35 USC § 112, First Paragraph

[11] The new matter rejection of claim(s) 8, 10, 26, 28, and 46 are rejected under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Regarding claims 8, 26, and 46, applicant argues this limitation is supported by the disclosure that "[d]uring structure determination...it was realized that the asymmetric unit comprised three HDAC-2-Zn2+-TSA molecules."

Applicant's argument is not found persuasive. Although applicant fails to point to where in the disclosure as filed the alleged descriptive support can be found, it appears that applicant is pointing to disclosure at p. 28, paragraph 118 of the specification. In this case, the "species" of the asymmetric unit of the crystal has three HDAC-2-Zn2+-

TSA molecules fails to support the genus of crystals of SEQ ID NO:5 optionally having any bound ligand and wherein the "protein is present in the protein crystal as a trimer." Even assuming *arguendo* the protein crystal is limited to a complex of HDAC-2-Zn2+-TSA, this disclosure would not support the limitations of claims 8, 26, and 46 for reasons that follow. According to Stedman's Online Medical Dictionary, the term "trimer" is defined as "[a] compound...made up of three components." Thus, the recitation of "the protein is present...as a trimer" suggests that the protein is made up of three components. However, a skilled artisan would recognize that the specification's disclosure of "[d]uring structure determination...it was realized that the asymmetric unit comprised three HDAC-2-Zn2+-TSA molecules" means the crystal has three molecules of HDAC-2-Zn2+-TSA per asymmetric unit – not that the protein of the crystal was made up of three components.

Regarding claims 10 and 28, applicant points to original claims 10 and 28 as providing descriptive support for the limitations at issue. However, this is not found persuasive, because, while the original claims may support the limitation of "a value less than 3.0 Angstroms," the original claims fail to provide support for the broader range of a value *equal to* or less than 3.0 Angstroms.

Applicant is invited to show support for the limitations at issue.

[12] The written description rejection of claim(s) 7-8, 10, 25-26, 28, 31, 45-46, and 49-52 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in the prior Office action. Claim

44 is included in the instant rejection for reasons that follow. Thus, claims 7-8, 10, 25-26, 28, 31, 44-46, and 49-52 are rejected.

RESPONSE TO ARGUMENT: Regarding claims 7 and 25, applicant argues the rejection is obviated by claim amendment to recite space group and unit cell dimensions.

Applicant's argument is not found persuasive. The examiner acknowledges the amendment to claim 7 and 25 to limit the claim so that the claim recites the sequence of the protein, the space group, and unit cell dimensions of the crystal. However, the examiner maintains the position that the specification fails to describe all crystallized proteins as encompassed by the claims. Claim 7 is drawn to a crystal comprising SEQ ID NO:5 with the recited space group and unit cell dimensions. In view of the transitional phrase "comprising," the examiner has interpreted the crystal as encompassing SEQ ID NO:5 and any other ligand(s) and for this reason, the claims encompass widely variant species. However, as noted in the prior Office action, the specification discloses only a single disclosed species of crystals, *i.e.,* a crystal of purified SEQ ID NO:5 in complex with TSA and Zn++ having the space group symmetry $P2_12_12_1$ and having vector lengths a=92.1 Å, b=97.6 Å, and c=138.9 Å and $\alpha=\beta=\gamma=90^\circ$ that diffracts x-rays to a resolution of 1.84 Å and has three molecules of SEQ ID NO:5 in complex with TSA and Zn++ per asymmetric unit; the specification discloses only a single representative species of the genus of crystallization methods, *i.e.,* the method disclosed at p. 52 of the specification; the specification discloses only a single representative species of crystal structures of SEQ ID NO:5, *i.e.,* the 3-D structure of SEQ ID NO:5 having the structural

coordinates of Figure 3; the specification discloses only a single representative species of methods of "rational drug design," *i.e.,* using the structure of SEQ ID NO:5 having the structural coordinates of Figure 3 to perform a fitting operation between an entity and the computer model and analyzing the results of the fitting operation to quantify the association between the entity and the model; and discloses only a single representative species of activities of the protein or a cell expressing the protein that can be measured, *i.e.,* histone deacetylase activity. As noted in the prior Office action, it is well-known in the art that a single polypeptide can have a plurality of distinct crystal forms, which one cannot predict *a priori* (see, *e.g.,* Aleshin et al. *FEBS Lett* 434:42-46, 1998). Thus, as noted in the prior Office action, the genus of proteins in crystalline form encompasses species that are widely variant, encompassing species of crystal species of unliganded and liganded forms of SEQ ID NO:5, wherein the liganded form is in complex with *any* ligand, methods of making, and structural coordinates and corresponding crystal structures thereof. However, other than the single species as noted above, the specification fails to describe any other crystals, methods for crystallization thereof, and crystal structures as encompassed by the claims. MPEP § 2163 states "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." As such, the single disclosed species of crystals, methods for making said crystal, and structural coordinates and corresponding crystal structures as noted above fail to describe all crystals and methods as encompassed by the claims.

Given the lack of description of a representative number of species, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

Claim 44 has been included in the instant rejection. Although the specification adequately describes the protein claimed "protein consisting of SEQ ID NO:5," the claim has been broadly, but reasonably interpreted according to MPEP § 2111 as encompassing a protein in crystallized form, particularly as the instant application is directed to protein crystals. However, for reasons discussed above, the single disclosed representative species of crystal fails to reflect the structural variation among the members of the genus. As noted in the prior Office action, there is no way to predict *a priori* the space group and unit cell dimensions of a protein, as evidenced by the references of Kierzek et al. (cited in the prior Office action; see cited relevant teachings) and Buts et al. (*Acta Crystallogr. D.*, vol. 61, pages 1149-1159, 2005), which teaches that even a single amino acid mutation can alter the space group symmetry and unit cell dimensions of a crystallized protein.

[13] The scope of enablement rejection of claim(s) 7-8, 10, 25-26, 28, 31, 45-46, and 49-52 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in the prior Office action. Claim 44 is included in the instant rejection for reasons that follow. Thus, claims 7-8, 10, 25-26, 28, 31, 44-46, and 49-52 are rejected.

RESPONSE TO ARGUMENT: Regarding claims 7 and 25, applicant argues the rejection is obviated by claim amendment to recite space group and unit cell dimensions.

Applicant's argument is not found persuasive. The examiner maintains the position that the specification, while being enabling for a crystal of purified SEQ ID NO:5 in complex with TSA and Zn++ having the space group symmetry $P2_12_12_1$ and having vector lengths a=92.1 Å, b=97.6 Å, and c=138.9 Å and $\alpha=\beta=\gamma=90^\circ$ that diffracts x-rays to a resolution of 1.84 Å and has three molecules of SEQ ID NO:5 in complex with TSA and Zn++ per asymmetric unit, a method for crystallization thereof at p. 52 of the specification, using the 3-D structure of SEQ ID NO:5 having the structural coordinates of Figure 3 to perform a fitting operation between an entity and the computer model and analyzing the results of the fitting operation to quantify the association between the entity and the model, and determining the effect of said entity by comparing the histone deacetylase activity of SEQ ID NO:5 or a cell expressing SEQ ID NO:5 in the presence and absence of the entity, does not reasonably provide enablement for all crystals, methods of crystallization, 3-D structures and uses thereof in "rational drug design," and activities of SEQ ID NO:5 or a cell expressing SEQ ID NO:5 that are measurable as broadly encompassed by the claims.

The breadth of the claims: The claims are so broad as to encompass: crystals of SEQ ID NO:5 that are unliganded or have any bound ligand, essentially any method of crystallization thereof, any 3-D conformation of SEQ ID NO:5, including homology models of unliganded or ligand-bound polypeptides, and any measurable "activity" of a

protein of SEQ ID NO:5 or a cell expressing SEQ ID NO:5. Also, as noted above, claim 44 has been broadly, but reasonably interpreted as encompassing a protein consisting of SEQ ID NO:5 in crystalline form. The broad scope of the claims is not commensurate with the enablement provided by the disclosure. In this case the disclosure is limited to a crystal of purified SEQ ID NO:5 in complex with TSA and Zn++ having the space group symmetry $P2_12_12_1$ and having vector lengths a=92.1 Å, b=97.6 Å, and c=138.9 Å and $\alpha=\beta=\gamma=90^\circ$ that diffracts x-rays to a resolution of 1.84 Å and has three molecules of SEQ ID NO:5 in complex with TSA and Zn++ per asymmetric unit, a method for crystallization thereof at p. 52 of the specification, using the 3-D structure of SEQ ID NO:5 having the structural coordinates of Figure 3 to perform a fitting operation between an entity and the computer model and analyzing the results of the fitting operation to quantify the association between the entity and the model, and determining the effect of said entity by comparing the histone deacetylase activity of SEQ ID NO:5 or a cell expressing SEQ ID NO:5 in the presence and absence of the entity.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: The state of the art at the time of the invention acknowledges a **high** level of unpredictability for making a protein crystal with an expectation that it is diffraction-quality. Branden et al. ("Introduction to Protein Structure Second Edition", Garland Publishing Inc., New York, 1999) teaches that "[c]rystallization is usually quite difficult to achieve" (p. 375) and that "[w]ell-ordered crystals...are difficult to grow because globular protein molecules are large, spherical, or ellipsoidal objects with irregular surfaces, and it is impossible to pack them into a crystal without forming large holes or

channels between the individual molecules" (p. 374). Also, Drenth ("Principles of X-ray Crystallography," Springer, New York, 1995) teaches that "[t]he science of protein crystallization is an underdeveloped area" and "[p]rotein crystallization is mainly a trial-and-error procedure" (p. 1). One cannot predict *a priori* those conditions that will lead to the successful crystallization of a diffraction-quality crystal nor can one predict the space group symmetry or unit cell dimensions of the resulting crystal. See Kierzek et al. (*Biophys Chem* 91:1-20, 2001), which teaches that "each protein crystallizes under a unique set of conditions that cannot be predicted from easily measurable physico-chemical properties" and that "crystallization conditions must be empirically established for each protein to be crystallized" (underline added for emphasis, p. 2, left column, top). Thus, in view of these teachings, a skilled artisan would recognize that it is highly unpredictable as to whether diffraction-quality crystals of other HDAC2 polypeptides optionally having a desired space group and unit cell dimensions as encompassed by the claims can be achieved using *any* crystallization parameters. Even assuming *arguendo* one can achieve diffraction-quality crystals, it is noted that Branden et al. teaches that only a few small proteins have been determined to a resolution of 1 Angstrom (p. 382, middle). Regarding the use of homology models for use in rational drug design, Lambert et al. (US Patent Application Publication 2004/0137518) acknowledges that "[p]otential or existent homology models cannot provide the necessary degree of specificity" in the *in silico* design of modulators (p. 3, ¶[0017]). See also the reference of Flower ("Drug Design, Cutting Edge Approaches," Royal Society of Chemistry, Cambridge, UK, 2002), which, addressing the use of homology models for

identifying lead drugs, discloses "[p]roblems still exist, however: the fitting together of protein domains in a multi-domain protein, the determination of the most likely conformation of protein loops, the correct positioning of amino acid side chains, flexible ligand docking - to name only a few" (p. 25, middle).

The amount of direction provided by the inventor; The existence of working examples: The specification discloses the utility of the claimed crystal is in the determination of the 3-D structure of HDAC2 and interacting molecules (p. 1, ¶[004]), which, as acknowledged by Branden et al. (*supra*) at p. 374, requires a diffraction-quality crystal. In this case, the specification discloses only a single working example of such a diffraction quality crystal, *i.e.*, a crystal of purified SEQ ID NO:5 in complex with TSA and Zn++ having the space group symmetry $P2_12_12_1$ and having vector lengths a=92.1 Å, b=97.6 Å, and c=138.9 Å and $\alpha=\beta=\gamma=90^\circ$ that diffracts x-rays to a resolution of 1.84 Å and has three molecules of SEQ ID NO:5 in complex with TSA and Zn++ per asymmetric unit; the specification discloses only a single working example of a method for successfully crystallizing the protein of SEQ ID NO:5, *i.e.*, the method disclosed at p. 52 of the specification; the specification discloses only a single working example of crystal structures of SEQ ID NO:5, *i.e.*, the 3-D structure of SEQ ID NO:5 having the structural coordinates of Figure 3; the specification discloses only a single working example of methods of "rational drug design," *i.e.*, using the structure of SEQ ID NO:5 having the structural coordinates of Figure 3 to perform a fitting operation between an entity and the computer model and analyzing the results of the fitting operation to quantify the association between the entity and the model; and discloses only a single

working example of activities of the protein or a cell expressing the protein that can be measured, *i.e.,* histone deacetylase activity. Other than these working examples, the specification fails to provide guidance regarding crystals, methods for crystallization, crystal structures, methods of rational drug design, and other activities of SEQ ID NO:5 or cells expressing SEQ ID NO:5 as encompassed by the claims.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of protein crystallography were known at the time of the invention, it was not routine in the art to screen all polypeptide complexes of SEQ ID NO:5 as encompassed by the claims for those that will yield diffraction-quality crystals using any crystallization conditions as encompassed by the claims and to determine those polypeptides that represent biologically-relevant HDAC2 structures.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required to make and use all crystals and polypeptides as broadly encompassed by the claims, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is

unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

[14] The rejection of claim 44 under 35 U.S.C. 102(e) as being anticipated by Venter (US Patent 6,812,339) and the rejection of claim 44 under 35 U.S.C. 102(b) as being anticipated by GenBank Accession Number Q92769, GI:3023939, February, 1998 are withdrawn in view of the amendment to limit the polypeptide to "[a] protein consisting of SEQ ID NO:5."

[15] Claim 44 is rejected under 35 U.S.C. 102(e) as being anticipated by Bressi et al. (US Patent 7,169,801). The claim is drawn to a protein consisting of SEQ ID NO:5. According to the specification (paragraph 211, pp. 51-52), SEQ ID NO:5 was created by trypsin digestion of a full length human HDAC-2 polypeptide fused to a C-terminal histidine tag.

The reference of Bressi et al. teaches an assay method comprising a step of contacting a full-length human HDAC-2 with a C-terminal histidine tag with trypsin (column 91, lines 55-60 and column 92, lines 50-62). This anticipates claim 44 as written.

While it is noted that the Bressi et al. reference fails to expressly teach a polypeptide having the amino acid sequence of SEQ ID NO:5, this polypeptide, *i.e.,* a polypeptide consisting of SEQ ID NO:5 would have necessarily been produced by the

method of Bressi et al. Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Claim Rejections - 35 USC § 101

[16] The rejection of claim 44 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues the rejection is obviated by amendment to recite "A protein consisting of SEQ ID NO:5," which is directed to non-statutory subject matter. However, this is not found persuasive because it is unclear as to the indication of the hand of man. Applicant fails to present any rationale or line f reasoning to support the assertion that claim 44 as amended is drawn to statutory subject matter. Apparently, applicant takes the position that the polypeptide of SEQ ID NO:5 is not naturally-occurring. However, while applicant may argue that the protein of claim 44 is not naturally-occurring by virtue of its being produced by trypsin cleavage, it is well-known that trypsin is naturally present in cells of the digestive system and would thus naturally cleave the polypeptide of SEQ ID NO:1 to yield the polypeptide of SEQ ID

NO:5. Applicant is requested to clarify how the claim as amended is now directed to statutory subject matter.

Claim Rejections – Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

[17] Claims 45-46 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22-31 and 42-51 of co-pending Application No. 10/826,134. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Claims 45-46 cannot be patentably distinct

over claims 22-31 and 42-51 of the '134 application when there is a specifically disclosed embodiment in the '134 application that supports claims 22-31 and 42-51 of that patent and falls within the scope of claims 45-46 herein because it would have been obvious to one of ordinary skill in the art to modify the method of claims 22, 27, 42, and 47 by selecting a specifically disclosed embodiment that supports that claim, *i.e.*, the method of claim 22, 27, 42, or 47, wherein the step of "creating a computer model..." (claim 22), "computing a computer model..." (claim 27), "constructing a computer model..." (claim 42), or "computing a computer model..." (claim 47) is accomplished by crystallizing the polypeptide of SEQ ID NO:5 to obtain a crystal having the space group symmetry $P2_12_12_1$ and having vector lengths a=92.1 Å, b=97.6 Å, and c=138.9 Å and $\alpha=\beta=\gamma=90^{\circ}$, with three molecules per asymmetric unit; performing x-ray diffraction to obtain a diffraction pattern and a crystal structure, which steps have been interpreted as being encompassed by "creating a computer model..." (claim 22), "computing a computer model..." (claim 27), "constructing a computer model..." (claim 42), or "computing a computer model..." (claim 47). One of ordinary skill in the art would have been motivated to do this because those embodiments are disclosed as being preferred embodiments within claims 22, 27, 42, and 47 of the '134 application. See particularly p. 48, paragraph 194 and pp. 52-53. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

[18] Status of the claims:

Claims 7-8, 10, 25-26, 28, 31, 44-46, and 49-52 are pending.

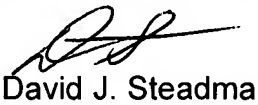
Claims 7-8, 10, 25-26, 28, 31, 44-46, and 49-52 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656